

Claims

1. A recombinant herpes simplex virus (HSV) particle having at least one protein on its surface, comprising:
 - (a) an altered viral surface protein, wherein the alteration reduces binding of the viral surface protein to a sulfated proteoglycan;
 - (b) an altered gD, wherein the alteration reduces binding of gD to one or more of its cellular receptors; and
 - (c) a heterologous peptide ligand on the surface of the recombinant HSV particle, the heterologous peptide ligand forming a fusion protein with the altered gD.
2. The recombinant HSV particle of claim 1, wherein the viral surface protein is gB.
3. The recombinant HSV particle of claim 1, wherein the viral surface protein is gC.
4. The recombinant HSV particle of claim 1, wherein the alteration of gD reduces binding to HveA.
5. The recombinant HSV particle of claim 1, wherein the alteration of gD reduces binding to HveC.
6. The recombinant HSV particle of claim 1, wherein the ligand forms a fusion protein with a viral surface protein.
7. The recombinant HSV particle of claim 6, wherein the ligand forms a fusion protein with gC.
8. The recombinant HSV particle of claim 1, wherein the ligand binds a receptor on the surface of a cell.
9. The recombinant HSV particle of claim 8, wherein the cell is a cancer cell.

10. The recombinant HSV particle of claim 9, wherein the cancer cell is a tumor cell.
11. The recombinant HSV particle of claim 9, wherein the cancer cell is a malignant glioma cell.
12. The recombinant HSV particle of claim 1, wherein the ligand is a cytokine.
13. The recombinant HSV particle of claim 12, wherein the cytokine is IL13.
14. The recombinant HSV particle of claim 1, wherein the ligand is a single-chain antibody.
15. A method of targeting a recombinant HSV particle to a cell comprising creating an HSV comprising a peptide ligand to a surface receptor specific to the cell, wherein the peptide ligand forms a fusion protein with an altered gD.
16. The method of claim 15, further comprising altering a viral surface protein, wherein the alteration reduces binding of the viral surface protein to a sulfated proteoglycan.
17. The method of claim 16, wherein the viral surface protein is gB.
18. The method of claim 16, wherein the viral surface protein is gC.
19. The method of claim 15, wherein the alteration to gD reduces binding of gD to at least one cellular receptor for gD.
20. The method of claim 19, wherein the alteration of gD reduces binding to HveA.
21. The method of claim 19, wherein the alteration of gD reduces binding to HveC.

22. The method of claim 21, wherein the ligand forms a fusion protein with gC.
23. The method of claim 15, wherein the cell is a cancer cell.
24. The method of claim 23, wherein the cancer cell is a tumor cell.
25. The method of claim 24, wherein the cancer cell is a malignant gliomal cell.
26. The method of claim 15, wherein the ligand is a cytokine.
27. The method of claim 26, wherein the cytokine is IL13.
28. The method of claim 15, wherein the ligand is a single-chain antibody.
29. A method of imaging a cell comprising:
 - (a) contacting the cell with a recombinant HSV particle comprising:
 - (i) an altered gD forming a fusion with a peptide ligand to a receptor specific to the cell; and
 - (ii) a gene encoding a marker protein; and
 - (b) detecting the presence of the marker protein.
30. The method of claim 29, wherein the cell is a cancer cell.
31. The method of claim 30, wherein the receptor is present at a higher number on the cancer cell as compared to a non-cancerous cell of the same type.
32. The method of claim 29, wherein the marker protein is thymidine kinase.
33. The method of claim 29, wherein the marker protein is green fluorescent protein.
34. The method of claim 29, wherein the marker protein luciferase.

35. A method of killing a target cell, comprising contacting the target cell with a recombinant HSV particle, wherein the HSV particle comprises an altered gD forming a fusion with a peptide ligand to a receptor specific to the cell.
36. A recombinant HSV comprising:
 - (a) a first gene encoding an altered viral surface protein, wherein the alteration reduces binding of the viral surface protein to a sulfated proteoglycan; and
 - (b) a second gene encoding an altered gD, wherein the alteration reduces binding of gD to one or more of its cellular receptors; and
 - (c) a coding region for a heterologous peptide surface ligand, wherein the coding region of the second gene and the coding region for a heterologous peptide surface ligand together encode a fusion protein comprising the altered gD and the heterologous peptide surface ligand.
37. The recombinant HSV of claim 36, wherein the viral surface protein is gB.
38. The recombinant HSV of claim 36, wherein the viral surface protein is gC.
39. The recombinant HSV of claim 36, wherein the alteration of gD reduces binding to HveA.
40. The recombinant HSV of claim 36, wherein the alteration of gD reduces binding to HveC.
41. The recombinant HSV of claim 36, wherein the ligand forms a fusion protein with a viral surface protein.
42. The recombinant HSV of claim 41, wherein the ligand forms a fusion protein with gC.
43. The recombinant HSV of claim 36, wherein the ligand binds a receptor on the surface of a cell.

44. The recombinant HSV of claim 43, wherein the cell is a cancer cell.
45. The recombinant HSV of claim 44, wherein the cancer cell is a tumor cell.
46. The recombinant HSV of claim 44, wherein the cancer cell is a malignant gliomal cell.
47. The recombinant HSV of claim 36, wherein the ligand is a cytokine.
48. The recombinant HSV of claim 47, wherein the cytokine is IL13.
49. The recombinant HSV of claim 36, wherein the ligand is a single-chain antibody.